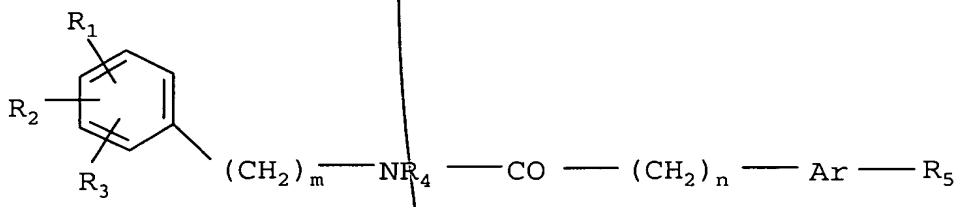
Patent Claims

1. Carboxylic acid amides of general formula



(I),

wherein
one of the groups m or n denotes the number 0 and
the other group m or n denotes the number 1,

Ar denotes a phenylene or naphthylene group optionally substituted by a fluorine, chlorine or bromine atom, by a trifluoromethyl, C_{1-3}-alkyl, hydroxy, C_{1-3}-alkoxy, phenyl-C_{1-3}-alkoxy, amino, C_{1-3}-alkylamino or di-(C_{1-3}-alkyl)-amino group, whilst the phenylene group may be substituted by another fluorine, chlorine or bromine atom or by another C_{1-3}-alkyl group,

a thienylene, thiazolylene, pyridinylene, pyrimidinylene, pyrazinylene or pyridazinylene group optionally substituted in the carbon skeleton by a C_{1-3}-alkyl group,

R_1 denotes a C_{1-3}-alkyl group optionally substituted by an amino, C_{1-3}-alkylamino, di-(C_{1-3}-alkyl)-amino, phenyl, naphthyl, heteroaryl or 4- to 7-membered cycloalkyleneimino group,

a C_{3-7}-cycloalkyl group which is substituted in the 1 position by a 5- to 7-membered cycloalkyleneiminocarbonyl group,

an amino, C_{1-5}-alkylamino, C_{5-7}-cycloalkylamino or phenyl-C_{1-3}-alkylamino group which may in each case be substituted at the amino-nitrogen atom by a benzoyl or phenylsulphonyl

group or by a C_{1-3}-alkyl or C_{1-3}-alkylcarbonyl group optionally substituted in the C_{1-3}-alkyl moiety by a carboxy group,

a 4- to 7-membered cycloalkyleneiminocarbonyl or cycloalkyleneiminosulphonyl group optionally substituted by a C_{1-3}-alkyl group,

an aminosulphonyl group optionally substituted by one or two C_{1-3}-alkyl groups,

a phenyl group optionally substituted by a fluorine, chlorine or bromine atom, by a trifluoromethyl, aminosulphonyl, C_{1-3}-alkyl or C_{1-3}-alkoxy group, which may additionally be substituted by a fluorine, chlorine or bromine atom or by a trifluoromethyl, C_{1-3}-alkyl or C_{1-3}-alkoxy group,

a C_{1-3}-alkoxy, phenyl-C_{1-3}-alkoxy, heteroaryloxy or heteroaryloxy-C_{1-3}-alkoxy group wherein the alkoxy moiety may be substituted in the 2 or 3 position in each case by an amino, C_{1-3}-alkylamino or di-(C_{1-3}-alkyl)-amino group,

a C_{3-7}-cycloalkoxy group, whilst the methylene group in the 3 or 4 position in a C_{5-7}-cycloalkoxy group may be replaced by an -NH group, whilst the -NH group may be substituted

by a C_{1-3}-alkyl group which may be substituted in the 2 or 3 position by an amino, C_{1-3}-alkylamino or di-(C_{1-3}-alkyl)-amino group, by a C_{1-3}-alkylcarbonyl, arylcarbonyl or arylsulphonyl group or

by an aminocarbonyl, C_{1-3}-alkylaminocarbonyl or di-(C_{1-3}-alkyl)-aminocarbonyl group, wherein in each case the oxygen atom of the carbonyl group is replaced by an imino group,

R_2 denotes a hydrogen, fluorine, chlorine or bromine atom, a C_{1-3}-alkyl, hydroxy or C_{1-3}-alkoxy group,

R_3 denotes a hydrogen atom or a C_{1-3}-alkyl group,

R_4 denotes a hydrogen atom or a C_{1-3}-alkyl group optionally substituted by a carboxy group and

R_5 denotes a cyano group or an amidino group optionally substituted by one or two C_{1-3}-alkyl groups, whilst

by the abovementioned heteroaryl groups is meant a 5-membered heteroaryl group optionally substituted by a C_{1-3}-alkyl group which contains, in the heteroaromatic moiety,

an imino group optionally substituted by a C_{1-3}-alkyl group, or an oxygen or sulphur atom,

an imino group optionally substituted by a C_{1-3}-alkyl group and an oxygen, sulphur or nitrogen atom,

an imino group optionally substituted by a C_{1-3}-alkyl group and two nitrogen atoms or

an oxygen or sulphur atom and two nitrogen atoms,

or a 6-membered heteroarylene group optionally substituted by a C_{1-3}-alkyl group which contains one or two nitrogen atoms in the heteroaromatic moiety,

the carboxy groups mentioned in the definition of the abovementioned groups may be replaced by a group which may be converted into a carboxy group *in vivo* or by a group which is negatively charged under physiological conditions or

the amino and imino groups mentioned in the definition of the abovementioned groups may be replaced by a group which may be cleaved *in vivo*,

the isomers and salts thereof.

2. Compounds of general formula I according to claim 1, wherein

one of the groups m or n denotes the number 0 and the other group m or n denotes the number 1,

Ar denotes a phenylene group optionally substituted by a fluorine, chlorine or bromine atom or by a methyl, hydroxy, methoxy or benzyloxy group, which may be substituted by another methyl group,

R_1 denotes a phenyl group optionally substituted by a fluorine, chlorine or bromine atom or by a trifluoromethyl, aminosulphonyl, C_{1-3}-alkyl or C_{1-3}-alkoxy group, which may additionally be substituted by a fluorine, chlorine or bromine atom or by a trifluoromethyl, C_{1-3}-alkyl or C_{1-3}-alkoxy group,

a methyl group substituted by a dimethylamino, pyrrolidino or imidazolyl group, wherein the imidazolyl moiety may be substituted by a methyl group,

an amino, C_{1-5}-alkylamino, cyclopentylamino or benzylamino group which may be substituted at the amino-nitrogen atom by a carboxy-C_{1-2}-alkyl, C_{1-3}-alkoxycarbonyl-C_{1-2}-alkyl, carboxy-C_{1-2}-alkylcarbonyl or C_{1-3}-alkoxycarbonyl-C_{1-2}-alkylcarbonyl group,

a benzoylamino or phenylsulphonylamino group,

a cyclopropyl group which is substituted in the 1 position by a 5- to 7-membered cycloalkyleneiminocarbonyl group,

an optionally methyl-substituted pyrrolidinocarbonyl, piperidinocarbonyl, pyrrolidinosulphonyl or piperidinosulphonyl group,

a C_{1-3}-alkoxy group wherein the alkoxy moiety in the 2 or 3 position may be substituted in each case by an amino, C_{1-3}-alkylamino or di-(C_{1-3}-alkyl)-amino group,

a phenyl-C_{1-3}-alkoxy or pyridinyloxy group,

a C_{5-7}-cycloalkoxy group wherein the methylene group in the 3 or 4 position may be replaced by an -NH group, whilst the -NH group may be substituted

by a C_{1-3}-alkyl or C_{2-3}-alkanoyl group,

by a C_{2-3}-alkanoyl or aminocarbonyl group wherein in each case the oxygen atom of the carbonyl group is replaced by an imino group,

R_2 denotes a hydrogen, fluorine, chlorine or bromine atom, a methyl, hydroxy or methoxy group,

R_3 denotes a hydrogen atom or a methyl group,

R_4 denotes a hydrogen atom or a methyl or ethyl group optionally substituted by a carboxy or C_{1-3}-alkoxycarbonyl group and

R_5 denotes a cyano group or an amidino group optionally substituted by a C_{1-6}-alkoxycarbonyl or benzoyl group,

the isomers thereof and the salts thereof.

3. Compounds of general formula I according to claim 1, wherein

one of the groups m or n denotes the number 0 and the other group m or n denotes the number 1,

Ar denotes a phenylene group optionally substituted by a methyl, hydroxy, methoxy or benzyloxy group,

R_1 denotes a phenyl group optionally substituted by a fluorine, chlorine or bromine atom or by a trifluoromethyl, aminosulphonyl, C_{1-3}-alkyl or C_{1-3}-alkoxy group, which may additionally be substituted by a fluorine, chlorine or bromine atom or by a trifluoromethyl, C_{1-3}-alkyl or C_{1-3}-alkoxy group,

a cyclopropyl group which is substituted in the 1 position by a 5- to 7-membered cycloalkyleneiminocarbonyl group, or a 4- to 7-membered cycloalkyleneiminocarbonyl group,

an optionally methyl-substituted pyrrolidinocarbonyl, piperidinocarbonyl or pyrrolidinosulphonyl group,

R_2 denotes a hydrogen, fluorine, chlorine or bromine atom or a methyl group,

R_3 denotes a hydrogen atom or a methyl group,

R_4 denotes a hydrogen atom or a methyl or ethyl group substituted by a carboxy, methoxycarbonyl or ethoxycarbonyl group and

R_5 denotes an amidino group optionally substituted by a C_{1-6}-alkoxycarbonyl or benzoyl group,

the isomers thereof and the salts thereof.

4. The following compounds of general formula I according to claim 1:

(a) 2-(5-carbamimidoyl-2-hydroxy-phenyl)-N-[3-methyl-4-(pyrrolidin-1-yl-carbonyl)-phenyl]-acetamide,

(b) 2-(2-benzyloxy-5-carbamimidoyl-phenyl)-N-(2-ethoxycarbonyl-ethyl)-N-[3-methyl-4-(pyrrolidin-1-yl-carbonyl)-phenyl]-acetamide,

(c) 2-(2-hydroxy-5-carbamimidoyl-phenyl)-N-(2-ethoxycarbonylethyl)-N-[3-methyl-4-(pyrrolidin-1-yl-carbonyl)-phenyl]-acetamide,

(d) 2-(2-hydroxy-5-carbamimidoyl-phenyl)-N-(2-carboxy-ethyl)-N-[3-methyl-4-(pyrrolidin-1-yl-carbonyl)-phenyl]-acetamide,

(e) 2-(5-carbamimidoyl-2-hydroxy-phenyl)-N-[3-methyl-4-(piperidin-1-yl-carbonyl)-phenyl]-acetamide and

(f) 2-(5-carbamimidoyl-2-hydroxy-phenyl)-N-[3-methyl-4-(2-aminosulphonyl-phenyl)-phenyl]-acetamide,

wherein the amidino group may additionally be substituted by a C_{1-6}-alkoxycarbonyl or benzoyl group, and the salts thereof.

5. 2-(5-Carbamimidoyl-2-hydroxy-phenyl)-N-[3-methyl-4-(pyrrolidin-1-yl-carbonyl)-phenyl]-acetamide and the salts thereof.

6. Physiologically acceptable salts of the compounds according to claims 1 to 5 wherein R_5 denotes one of the amidino groups mentioned in claims 1 to 5.

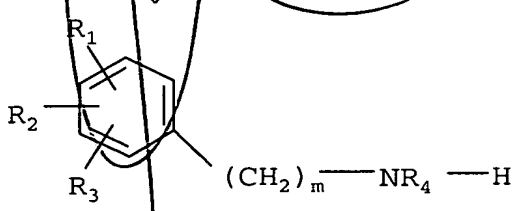
7. Pharmaceutical compositions containing a compound according to at least one of claims 1 to 5, wherein R_5 denotes one of the amidino groups mentioned in claims 1 to 5, or a salt according to claim 6 optionally together with one or more inert carriers and/or diluents.

8. Use of a compound according to at least one of claims 1 to 5, wherein R_5 denotes one of the amidino groups mentioned in claims 1 to 5, or a salt according to claim 6, for preparing a pharmaceutical composition having an anti-thrombotic activity.

9. Process for preparing a pharmaceutical composition according to claim 7, characterised in that a compound according to at least one of claims 1 to 5, wherein R_5 denotes one of the amidino groups mentioned in claims 1 to 5, or a salt according to claim 6 is incorporated in one or more inert carriers and/or diluents by a non-chemical method.

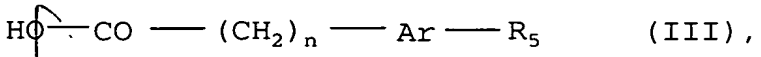
10. Process for preparing the compounds according to claims 1 to 6, characterised in that

a) a compound of general formula



(II),

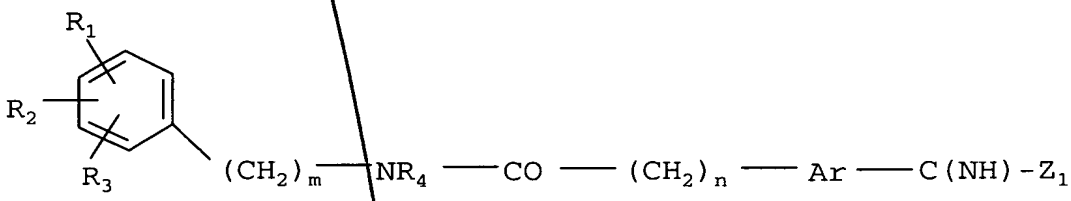
wherein
R_1 to R_4 and m are defined as in claims 1 to 5, is acylated with a carboxylic acid of general formula



(III),

wherein
Ar, R_5 and n are defined as in claims 1 to 5, or with the reactive derivatives thereof, or

b) in order to prepare a compound of general formula I wherein R_5 denotes an amidino group which may be substituted by one or two C_{1-3}-alkyl groups, a compound of general formula



(IV),

optionally formed in the reaction mixture,
wherein
R_1 to R_4, Ar and n are defined as in claims 1 to 5 and
Z_1 denotes an alkoxy, aralkoxy, alkylthio or aralkylthio group, is reacted with an amine of general formula

, (V)

wherein
R_6 and R_7, which may be identical or different, each denote a hydrogen atom or a C_{1-3}-alkyl group, or with the salts thereof, and

subsequently, if desired, a compound of general formula I thus obtained which contains an amino or imino group is converted by means of a corresponding acyl derivative into a corresponding acyl compound of general formula I and/or

a compound of general formula I thus obtained which contains an esterified carboxy group is converted by hydrolysis into a corresponding carboxylic acid of general formula I and/or

a compound of general formula I thus obtained which contains a carboxy group is converted by esterification into a corresponding ester and/or

a protecting group used to protect reactive groups during the reactions is cleaved and/or

a compound of general formula I thus obtained is resolved into the stereoisomers thereof, and/or

a compound of general formula I thus obtained is converted into the salts thereof, particularly, for pharmaceutical use, into the physiologically acceptable salts thereof with an inorganic or organic acid or base.

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